NCBI GTeX eQTL Browser Tutorial

eQTL Overview:

An expression quantitative trait locus (eQTL) represents a marker (locus) in the genome in which variation between individuals is associated with a quantitative gene expression trait, often measured as mRNA abundance. Thus, the three critical components to eQTL results are 1) the genotypes at a marker (here a SNP), 2) the gene expression levels, as measured by a probe or sequence information, and 3) a measure of the statistical association between the two in a study population, such as the p-value. The eQTL browser described here provides a means to query a database of eQTL results, applying filters based on the above types of data. It should be recognized that a substantial number of tests are performed, and that the significance of p-values should be considered in this multiple testing context.

eQTLs can be described as being cis, where the genotyped marker is near, perhaps within 2 MB, of the expressed gene, or trans, in which the genotyped marker is distant from the expressed gene or even on another chromosome. Currently only the cis-eQTLs from the Stranger et al. paper are displayed, although in the future trans will be displayed as well.

eQTL Browser Tutorial:

Upon initial loading, the GTEx webpage displays two sections:

Current Dataset Information – a description of the current dataset

Search Parameters – allows a user to build complex queries

Use case 1: Display top eQTL results - To display the most significant associations within the dataset

Accept the default parameters by leaving blank the Search Parameters form.

Mouse-click on the **_Display Results_** buttons either above or below the search form.

The Search Results table will now be displayed; it is comprised of three primary header sections:

SNP - SNP marker name and position

Probe - Probe name, position, gene name, and mRNA splice variant list

Statistics – P-value and other test statistics related to the test of association between SNP genotype and gene expression.

The final column *Description* provides additional details of probe annotation.

The GTEx (Genotype-Tissue Expression) eQTL Browser screenshot showing Search Results with 12,399 results.

Search Results (1 - 50 of 12399)

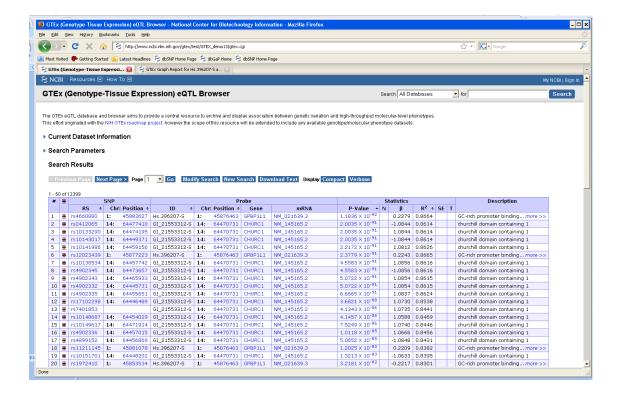| #		SNP RS	Chr: Position	Probe ID	Chr: Position	Gene	mRNA	P-Value	N	β	R²	SE	T	Description
1		rs4660880	1: 45883627	Hs.396207-S	1: 45876463	GPBP1L1	NM_021639.3	1.1836×10^{-92}		0.2279	0.8664			GC-rich promoter binding... *more >>*
2		rs2412065	14: 64477410	GI_21553312-S	14: 64470731	CHURC1	NM_145165.2	2.0035×10^{-91}		-1.0844	0.8614			churchill domain containing 1
3		rs10133290	14: 64474195	GI_21553312-S	14: 64470731	CHURC1	NM_145165.2	2.0035×10^{-91}		1.0844	0.8614			churchill domain containing 1
4		rs10143017	14: 64449371	GI_21553312-S	14: 64470731	CHURC1	NM_145165.2	2.0035×10^{-91}		-1.0844	0.8614			churchill domain containing 1
5		rs10141986	14: 64459156	GI_21553312-S	14: 64470731	CHURC1	NM_145165.2	2.2172×10^{-91}		1.0812	0.8626			churchill domain containing 1
6		rs12023439	1: 45877223	Hs.396207-S	1: 45876463	GPBP1L1	NM_021639.3	2.3779×10^{-91}		0.2243	0.8665			GC-rich promoter binding... *more >>*
7		rs10138534	14: 64457742	GI_21553312-S	14: 64470731	CHURC1	NM_145165.2	4.5583×10^{-91}		1.0856	0.8616			churchill domain containing 1
8		rs4902345	14: 64473657	GI_21553312-S	14: 64470731	CHURC1	NM_145165.2	4.5583×10^{-91}		-1.0856	0.8616			churchill domain containing 1
9		rs4902343	14: 64465933	GI_21553312-S	14: 64470731	CHURC1	NM_145165.2	5.0722×10^{-91}		1.0854	0.8615			churchill domain containing 1
10		rs4902332	14: 64445731	GI_21553312-S	14: 64470731	CHURC1	NM_145165.2	5.0722×10^{-91}		1.0854	0.8615			churchill domain containing 1
11		rs4902335	14: 64455651	GI_21553312-S	14: 64470731	CHURC1	NM_145165.2	6.6665×10^{-91}		1.0837	0.8624			churchill domain containing 1
12		rs17102298	14: 64446489	GI_21553312-S	14: 64470731	CHURC1	NM_145165.2	3.6821×10^{-88}		1.0730	0.8538			churchill domain containing 1
13		rs7401853		GI_21553312-S	14: 64470731	CHURC1	NM_145165.2	4.1343×10^{-86}		1.0735	0.8441			churchill domain containing 1
14		rs10148687	14: 64454029	GI_21553312-S	14: 64470731	CHURC1	NM_145165.2	4.1457×10^{-86}		1.0588	0.8469			churchill domain containing 1
15		rs10149617	14: 64471914	GI_21553312-S	14: 64470731	CHURC1	NM_145165.2	7.5249×10^{-86}		1.0740	0.8446			churchill domain containing 1
16		rs4902336	14: 64457015	GI_21553312-S	14: 64470731	CHURC1	NM_145165.2	1.0118×10^{-85}		1.0666	0.8456			churchill domain containing 1
17		rs4899152	14: 64456869	GI_21553312-S	14: 64470731	CHURC1	NM_145165.2	5.0652×10^{-85}		-1.0848	0.8431			churchill domain containing 1
18		rs11211145	1: 45881078	Hs.396207-S	1: 45876463	GPBP1L1	NM_021639.3	1.2025×10^{-83}		0.2209	0.8382			GC-rich promoter binding... *more >>*
19		rs10151701	14: 64448202	GI_21553312-S	14: 64470731	CHURC1	NM_145165.2	1.3213×10^{-83}		-1.0633	0.8395			churchill domain containing 1
20		rs1972410	1: 45853534	Hs.396207-S	1: 45876463	GPBP1L1	NM_021639.3	3.2181×10^{-82}		-0.2217	0.8301			GC-rich promoter binding... *more >>*

Result sets can be very large: the search above resulted in 12,399 results, with only the first 1-50 displayed. Search results can be paged through using the **Next Page** and **Previous Page** buttons. The **Download Text** button will download a tab delimited results file.
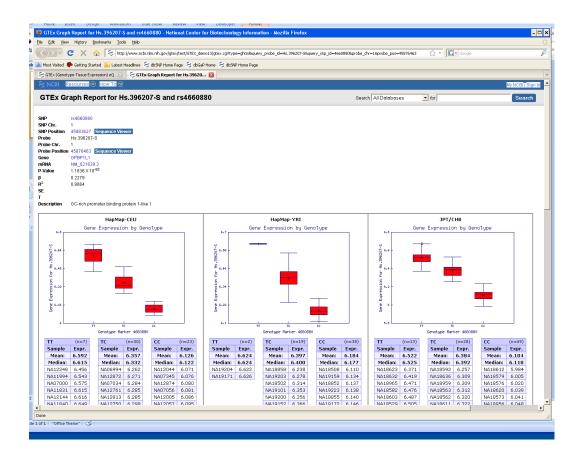
Above the Search Result table, you will see that **Current Dataset Information** and **Search Parameters** have now been collapsed. Clicking on the arrow next to each will expand it. Specifically, **Search Parameters** can be expanded to review the previous search or to enter new search parameters. Clicking **Display Results** again will refresh the search results with the new query.

Detailed Results View

A detailed "GTEx Graph report" for each row in the results table can be accessed by clicking either the box-plot icon in the second column or the P-value column.

The GTeX Graph report page contains summary information for the selected row, and a series of genotype/expression box-plots for each tested population. These box-plots contain the three genotype class categories on the horizontal axis and log normalized expression value on the vertical axis.

Below each graph the expression values for each sample is displayed in tables.

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http://www.ncbi.nlm.nih.gov/gtex/test/GTEX_demo13/gtex.cgi?type=ghtml&query_probe_id=Hs.396207-S&query_snp_id=4660880&probe_chr=1&probe_pos=45876463

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GTEx Graph Report for Hs.396207-S and rs4660880   Search   All Databases   for   Search

SNP	rs4660880
SNP Chr.	1
SNP Position	45883627 Sequence Viewer
Probe	Hs.396207-S
Probe Chr.	1
Probe Position	45876463 Sequence Viewer
Gene	GPBP1L1
mRNA	NM_021639.3
P-Value	1.1836×10^{-92}
β	0.2279
R^2	0.8664
SE	
T	
Description	GC-rich promoter binding protein 1-like 1

HapMap-CEU — Gene Expression by Genotype

HapMap-YRI — Gene Expression by Genotype

JPT/CHB — Gene Expression by Genotype

HapMap-CEU:

TT	(n=7)	TC	(n=30)	CC	(n=23)
Sample	Expr.	Sample	Expr.	Sample	Expr.
Mean:	6.592	Mean:	6.357	Mean:	6.126
Median:	6.615	Median:	6.332	Median:	6.122
NA12248	6.456	NA06994	6.262	NA12044	6.071
NA11994	6.543	NA12872	6.271	NA07345	6.076
NA07000	6.575	NA07034	6.284	NA12874	6.080
NA11831	6.615	NA12761	6.285	NA07056	6.081
NA12144	6.616	NA12813	6.285	NA12005	6.086
NA11840	6.649	NA12750	6.298	NA12057	6.095

HapMap-YRI:

TT	(n=2)	TC	(n=19)	CC	(n=38)
Sample	Expr.	Sample	Expr.	Sample	Expr.
Mean:	6.624	Mean:	6.397	Mean:	6.184
Median:	6.624	Median:	6.400	Median:	6.177
NA19204	6.622	NA18858	6.238	NA18508	6.110
NA19171	6.626	NA19203	6.278	NA18159	6.134
		NA18502	6.314	NA18852	6.137
		NA19101	6.353	NA19223	6.138
		NA19200	6.356	NA18855	6.140
		NA19152	6.366	NA19172	6.146

JPT/CHB:

TT	(n=13)	TC	(n=28)	CC	(n=49)
Sample	Expr.	Sample	Expr.	Sample	Expr.
Mean:	6.522	Mean:	6.384	Mean:	6.104
Median:	6.525	Median:	6.392	Median:	6.110
NA18623	6.371	NA18592	6.257	NA18612	5.984
NA18632	6.419	NA18636	6.309	NA18579	6.005
NA18965	6.471	NA18959	6.309	NA18576	6.020
NA18582	6.476	NA18563	6.312	NA18620	6.039
NA18603	6.487	NA18562	6.320	NA18573	6.041
NA18529	6.505	NA18611	6.322	NA18956	6.048

Done

Clicking on the **Sequence Viewer** buttons by the SNP and Probe positions near the top of the page will bring the user to the NCBI sequence viewer, zoomed to that region.

Use case 2: Search by Gene(s) of interest - To display significant eQTLs for a gene(s) of interest
On the right side of the **Search Parameters** form there is a text box labeled *Gene Symbols or ID numbers.*

A list of gene symbols or Refseq identifiers can be input, separated by spaces of on different lines, into this box in order to search for eQTL results showing association with expression of those genes.   To input a text file, rather than pasting into that text box, users may click on the "Browse" button and select a file to upload.   Genes can also be selected by specifying a chromosome and position range.

Clicking **Display Results** will then search the eQTL results limited to this set of gene expression traits.

Use case 3: Search by SNPs of interest - To display significant gene expression traits associated with a SNP of interest
Similarly, the eQTL result dataset can be queried by a list of SNPs in the box, a set of SNPs uploaded in a file, or by SNPs position, under the **SNP filters** part of the Search Parameters form, on the right side.

Use case 4: Combination search, p-value threshold, and sorting.
Both a list of SNPs and expression of a set of Genes can be queried simultaneously, combining case 2 and case 3 above. A filter on the p-value significance, beyond the default 10^-5 level, can be applied by

selecting the exponent using the drop down list on the bottom left of the Search Parameters form. Output is automatically sorted by P-value, but can be also be sorted by SNP or gene position, or names, using the controls on the bottom right.